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**Review**

# Photosensitisation of livestock grazing *Narthecium ossifragum*: Current knowledge and future directions

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**Abstract**

Photosensitisation diseases can cause production and animal welfare losses world-wide. In North-West Europe a photosensitisation disease complex known as ‘plochteach’, ‘yellowses’, ‘saut’ and ‘alveld’ occurs in lambs on extensive pastures containing bog asphodel (*Narthecium ossifragum*). Affected lambs develop lesions on the ears, face and sometimes the back, with erythema, oedema, ulceration and necrosis that can be followed by secondary infection and death. Adult sheep appear unaffected and the incidence in lambs varies from year to year with variations in susceptibility between- and within- breeds. The definitive cause remains uncertain although ingestion of *N. ossifragum*, which contains hepatotoxic saponins, has been implicated in the aetiology. However, problems replicating the disease complex by feeding *N. ossifragum* in a controlled environment have led to alternative hypotheses, including possible intake of toxins from fungal spores and cyanobacteria. Further research is required to assess the putative role of *N. ossifragum*, the scale of economic and animal welfare losses associated with the disease, how best to identify affected animals before external clinical signs appear and the treatment and management of clinical cases. Given the challenges involved in isolating the causative agent(s) of plochteach, an animal breeding route may be effective if heritability of resistance/susceptibility can be demonstrated.

*Keywords:* Lambs; Extensive pastures; Liver damage; Plochteach; Alveld; Secondary photosensitisation

## Introduction

Many photosensitisation diseases in livestock cause animal welfare and economic losses worldwide (Table 1) (Kellerman et al., 1994; Cheeke, 1995; Flåøyen, 2000). For example, annual costs of facial eczema (pithomycotoxicosis) in New Zealand in the 1980s were estimated at NZ$53M[1] to NZ$63+M (Anonymous, 1990; Towers, 1986). Annual economic costs of geeldikkop (an acute photodynamic disease in sheep in South Africa) were estimated at over 13M Rand[2] in the 1990s (Kellerman et al., 1996).

In North-West Europe a photosensitisation disease complex prevalent in wet upland environments, where extensively-grazed sheep are the dominant livestock species, has not yet been satisfactorily addressed in spite of a considerable amount of research, particularly in Norway. The disease complex is known as 'plochteach' (pronounced 'ploch-tea') and is also called 'yellowses', 'big head', 'head greet', 'hard lug' and 'saut' in different parts of the UK (Ender, 1955; Ford, 1964; Malone et al., 1992; Flåøyen, 1993). In Norway, an identical complex is known as 'alveld' (Ender, 1955) and is regarded as an important sheep health issue (Ulvund, 2012). In this paper we refer to this North-West European photosensitisation disease complex as plochteach.

Photosensitisation occurs when abnormal quantities of photodynamic agents are present in the blood, resulting in skin oedema, ulceration and necrosis (Rowe, 1989; Sargison, 2008) with secondary infections commonly occurring. Primary photosensitisation (Table 1) results from the accumulation of a photodynamic chemical in the blood. Secondary (or hepatogenous) photosensitisation (Table 1) occurs when toxins damage the liver, limiting its

[1] NZ$1 = approx. £0.43, €0.60, US$0.62 at 11 July 2015

[2] ZAR1 = approx. £0.05, €0.07, US$0.08 at 11 July 2015

ability to remove photodynamic chemicals derived from chlorophyll from the blood (Cheeke, 1995). Plochteach is an example of secondary photosensitisation (Ender, 1955; Flåøyen et al., 1991a; Flåøyen, 1993). A wide range of chemicals can act as photosensitizing agents, including those that are plant, fungal and bacterial in origin, but most of the important causes of photosensitivity in grazing livestock are derived from plants (Rowe, 1989).

Our understanding of plochteach, and observation of its incidence, has been constrained by the nature of the extensive farming systems where the disease is found. Most breeding ewes in North-West Europe graze unsupervised on unfenced hilly or mountainous terrain (Waterhouse, 1996; Asheim and Mysterud, 1999; Morgan-Davies et al., 2012; Scottish Government, 2014) and in Scotland the sheep are gathered only four to six times a year (Waterhouse, 1996; Morgan-Davies et al., 2012). Ewe mortality in West and North-West Highland hill sheep is in the range 10 – 12% (Morgan-Davies et al., 2008; Craig, 2014) but lamb losses can only be estimated as they are not marked at birth and scavengers quickly dismember and remove carcasses.

**Hypothesised aetiology**

The aetiology of plochteach is currently unknown, but the plant bog asphodel (*Narthecium ossifragum* (L.) Hudson), mycotoxins (Flåøyen, 1993) and cyanobacteria have been proposed as possible causes. It is possible that the disease only occurs when two or more causal agents work in synergy. Attempting to isolate the toxin(s) causing plochteach continues to be a research goal.

*Bog asphodel (Narthecium ossifragum)*

In 1955, Ender found saponins in *N. ossifragum* that are associated with other secondary photosensitisation diseases elsewhere in the world (Kellerman et al., 1996; Miles et al., 1992), and suggested these could be the cause of the disease. Some dosing experiments using concentrated extracts from *N. ossifragum* have replicated the disease (Ender, 1955; Abdelkader et al., 1984), but other work using concentrated extract or feeding cut, unprocessed, *N. ossifragum* did not (Ender, 1955; Flåøyen et al., 1991b).

An investigation on a very small sample of young calves suggested that consumption of *N. ossifragum* flower stems may be more likely to cause liver damage than consumption of the leaves and that the hepatotoxin may be present in the insoluble residue of the plant (Flåøyen et al., 1997). Scientific (Mysterud et al., 2007a) and anecdotal (Laksesvela and Dishington, 1983) evidence suggests that not all pastures containing *N. ossifragum* are toxic, and it has been proposed that ingestion of *N. ossifragum* alone does not necessarily cause plochteach (Aas and Ulvund, 1989). Although *N. ossifragum* saponins have been found to be more concentrated in samples from Scottish plants than Norwegian ones (Wilkins et al., 2004), the disease does not appear to be more severe in Scotland than in Norway.

Mysterud et al. (2007a) studied two naturally occurring outbreaks of plochteach in Norway and concluded that saponins alone are unlikely to be the sole cause of the disease. A 5-year study by Laksesvela and Dishington (1983) found that the saponin content within *N. ossifragum* plants did not change over the growing season. As plochteach outbreaks only occur in early to mid-summer, at least one other factor may be involved in the aetiology (Ender, 1955; di Menna et al., 1992).

*Nephrotoxicity of Narthecium ossifragum and recorded cattle poisoning incidents*

*N. ossifragum* contains 3-methoxy-2(*5H*)-furanone (Langseth et al., 1999) which has been shown to be nephrotoxic in cattle (Malone et al., 1992; Flåøyen et al., 1995a; 1995b; Angell and Ross, 2011), sheep (Flåøyen et al., 1995c; 2001), moose (Vikøren et al., 1999), reindeer and red deer (Flåøyen et al., 1999) and goats (Wisløff et al., 2003). *N. ossifragum* associated poisoning in cattle was first reported in Northern Ireland (Malone et al., 1992) and subsequently in Norway (Flåøyen, 1995a) and North Wales (Angell and Ross, 2011). Although cattle can be severely affected, photosensitisation is not a feature of *N. ossifragum* intoxication in this species.

*Bog asphodel (Narthecium ossifragum) description*

*N. ossifragum* (Fig. 1), a deciduous perennial herb found in North-West Europe (Summerfield, 1974; Preston et al., 2002), is widespread and common in the north and west of Britain (Clapham et al., 1987) but absent from much of central and eastern England (Preston et al., 2002). It occurs in a wide range of habitats especially where there is some soil water movement and can dominate mire communities (Summerfield, 1974; Rodwell, 1991, 1992) but is intolerant of shade (Preston et al., 2002).

*N. ossifragum* has been ranked 6th, 5th and 4th most palatable of nine mire species (Pollock et al., 2007). It persists in grazed environments but has been observed to flower more vigorously and increase in abundance after the total cessation of grazing by large herbivores (Rawes, 1983). Anecdotal information suggests increases in abundance of *N. ossifragum* can result from reduced grazing in upland North-West England where reduced winter (and spring) grazing is common. In some places moorland drains are blocked in order to raise water tables, and this increases the habitat favourable for the plant. Whilst reduced grazing may have an impact on the plant, no quantitative or clinical analysis appears to have been carried out.

136

137 *Mycotoxins*

138 Various mycotoxins on or in forage plants are known to cause poisoning of grazing
139 animals worldwide (Cheeke, 1995). Fungal toxins, either alone or interacting with *N.*
140 *ossifragum* toxins, may be involved in the aetiology of plochteach. Fungi infecting *N.*
141 *ossifragum* plants, neighbouring plants or saprophytic fungi on dead plant material nearby
142 have been studied, but no evidence has concluded that they cause plochteach or contribute to
143 its aetiology. Fungi studied include *Cladosporium* spp., *Fusarium* spp., *Penicillium* spp.,
144 *Trichoderma* spp. (Mysterud et al., 2007b), *Cladosporium magnusianum* (di Menna et al.,
145 1992; Flåøyen et al., 1993) and *Pithomyces chartarum* (Aas and Ulvund, 1989; di Menna et
146 al., 1992; Flåøyen et al., 1993; Mysterud et al., 2007b). *P. chartarum* has been shown to cause
147 facial eczema, a hepatogenous photosensitisation disease in New Zealand (Morris et al., 2004)
148 and although detected in Great Britain (Lacey and Gregory, 1962; Gregory and Lacey, 1964)
149 and Norway, the fungus is not sufficiently abundant to be a likely cause of plochteach (Lacey,
150 1975; di Menna et al., 1992).

151

152 *Cyanobacteria*

153 The presence of primary photosensitising agents derived from biofilms (such as mats
154 of cyanobacteria) in drinking water available to lambs has recently been hypothesised as a
155 causal agent or contributory factor to plochteach (Tønnesen et al., 2013). Water samples
156 drawn from a plochteach-prone area were shown to contain phycocyanins (chromophores
157 from cyanobacteria) that can produce large quantities of singlet oxygen (a free radical)
158 capable of damaging cells (Tønnesen et al., 2013). This suggests that plochteach may result
159 from primary as well as secondary photosensitisation (Tønnesen et al., 2010). Cyanobacteria

in drinking water have been demonstrated to cause liver damage and photodermatitis and death in sheep and cattle in South Africa (van Halderen et al., 1995).

**Pathogenesis**

The pigment chlorophyll, ingested whenever green plant material is eaten, is broken down into phylloerythrin (also known as phytoporphyrin) by microorganisms in the rumen (Flåøyen, 2000). Normally any phylloerythrin that is absorbed into the hepatic circulatory system (Tennant, 1998) is excreted via the bile duct and gall bladder (Morris et al., 2009). It is thought that toxins from *N. ossifragum* (and/or other possible sources) damage the liver cells and inhibit the excretion of phylloerythrin (Dishington and Laksesvela, 1976) which then accumulates in the general circulatory system, and in exposed areas produces free radicals that can damage skin cells (Henderson, 1990; Cheeke, 1995; Baird, 2000).

Liver pathology in cases of plochteach is characterised by hepatocellular damage (Wisløff et al., 2002) and bile duct proliferation rather than obstruction (Flåøyen et al., 1991a). No macroscopic liver damage has been reported but there was hepatocellular single cell necrosis and modest portal fibroplasia with accumulation of glycogen and neutrophils (Flåøyen et al., 1991a). Laksesvela and Dishington (1983) found liver damage up to 7 days before the appearance of clinical signs in many lambs but their test required an IV injection of bromsulphthalein followed by a blood test 7 days later so is clearly impractical under extensive grazing systems. Wisløff et al. (2002) found elevated plasma conjugated bilirubin in 14/16 photosensitised lambs, with concentrations of glutamate dehydrogenase (GLDH), a mitochondrial enzyme used to evaluate the extent of parenchymal liver damage, to be normal in the majority of photosensitised lambs and aspartate aminotransferase (AST) elevated in

<50%. A quick, simple and minimally invasive liver function test is needed to identify lambs with pre-clinical plochteach.

**Clinical signs of plochteach**

Clinical signs have been observed in lambs but not in adult sheep (Flåøyen, 1993) and include oedema, serum exudation, ulceration and necrosis (Scott, 2007) in areas where blood vessels are close to the surface of exposed skin (lips, ears, eyelids, back). Skin sloughing can lead to partial or full ear loss, making tagging impossible. Bald patches often appear along the skin over the spine where the fleece splits. There is a high risk of secondary infection. Animals with plochteach become dull, cease eating, seek shade and often damage the skin further by rubbing or kicking their head (Scott, 2007). In severe cases animals may die from shock or from secondary infection.

In Norway, clinical signs of the disease have been seen 10-14 days (Ender, 1955) and 15-56 days (Wisløff et al., 2002) after lambs were given access to pasture containing *N. ossifragum*. In Scotland (G.V. Cuthill, unpublished data) and Norway (Ender, 1955; Flåøyen et al., 1991b) and from our own observations, outbreaks tend to occur in June and July. In Norway the timing of outbreaks has been reported to vary from year to year and with altitude and latitude, with late May being the earliest reported disease onset (Ender, 1955). Little else is known about the time-course of the disease.

**Diagnosis and differential diagnoses**

Diagnosis is based on the clinical signs in a lamb that has been grazing on pasture containing *N. ossifragum*. Photosensitised lambs that have been grazing on *N. ossifragum*-free pasture may have been poisoned by other plants such as forage rape (*Brassica napus*) or

*Hypericum perforatum* (St John's wort) (Table 1). Severe cobalt deficiency (ovine white liver disease) can also cause photosensitisation (Suttle and Jones, 2007) and should be excluded.

Although there has been one report of photosensitivity in cattle in Europe as a result of liver fluke (*Fasciola hepatica*) disease (Flock et al., 2003), fascioliasis has not been associated with photosensitisation in livestock in Britain. Moreover, *Galba truncatula* (formerly *Lymnaea truncatula*), the snail that is the intermediate host for *Fasciola hepatica*, is very uncommon on the acidic pastures where plochteach occurs (Kerney, 1999). The lancet fluke (*Dicrocoelium dendriticum*) has been associated with photosensitisation of sheep in Scotland (Sargison et al., 2012), but is not commonly seen in Britain.

**Treatment**

There is currently no specific treatment for animals affected with photosensitisation other than supportive therapies such as placing animals in the dark[3] for up to 3 weeks[4] and providing them with chlorophyll-free hay[5]. Administering corticosteroids in early stages will reduce oedema (Scott, 2007). Recovery from photosensitisation is possible (Scott, 2007), with duration dependant on the severity of the case. Putting affected lambs in dark sheds or shady woodlands is impractical in many situations where grazing is extensive and a large number of lambs affected.

[3] See: NADIS, 2015. Non-parasitic skin conditions in sheep. http://www.nadis.org.uk/bulletins/non-parasitic-skin-conditions-in-sheep.aspx (accessed 3 July 2015).

[4] See: Farmers Weekly, 2002. Photosensitisation. http://www.fwi.co.uk/livestock/photosensitisation.htm (accessed 3 July 2015).

[5] See: Robson, S., 2007. New South Wales Department of Primary Industries Primefact 449: Photosensitisation in stock. http://www.dpi.nsw.gov.au/agriculture/livestock/sheep/health/photosensitisation-stock (accessed 3 July 2015).

In New Zealand facial eczema is treated with the provision of shade, water and a low-protein diet with little chlorophyll (i.e. hay or silage). Dosing with zinc (which reduces the availability of the toxin) is recommended but copper supplements that can aggravate the disease should be avoided[6]. However since a different toxin causes facial eczema, it is not known whether zinc supplementation would have any effect on plochteach. In extensive grazing systems, the low frequency of inspection can limit the potential for timely intervention.

**Epidemiology**

Photosensitisation of lambs grazing *N. ossifragum*-containing pastures has been reported from Norway, the Faroe Islands and the British Isles (Flåøyen et al., 2003) but the disease does not appear to be a major problem elsewhere in Europe. The disease was first reported in the literature by Jessen (1893; cited by Flåøyen, 1993) and studied in 1908 by Kjoss-Hansen (1910; cited by Flåøyen, 1993). *N. ossifragum* has been associated with the disease since 1916 (Kjoss-Hansen, 1918; cited by Flåøyen, 1993). In the UK, McGowan (1919) referred to the disease as 'cholera of the sheep' and directly associated it with *N. ossifragum*.

The disease complex is thought to be highly prevalent in the West and North-West Highlands of Scotland where *N. ossifragum* is abundant (Rodwell, 1991; 1992). Records of Scottish Blackface lambs with clinical plochteach were collated from Scotland's Rural College (SRUC) farms at Kirkton and Auchtertyre in Perthshire, Scotland in the summers of 2013 and 2014. In 2013, 3.5% of Kirkton lambs and 10.8% of Auchtertyre lambs had clinical

[6] See: Beef and Lamb New Zealand, 2011. Facing up to facial eczema. http://www.beeflambnz.com/Documents/Farm/Facing%20up%20to%20facial%20eczema.pdf (accessed 3 July 2015).

252 signs of the disease (G.V. Cuthill, unpublished data). In 2014, 2.6% of Kirkton lambs and
253 20.4% of Auchtertyre lambs were affected. In 2014 around one-third of the affected animals
254 from both flocks had disappeared by weaning (late August) and presumably died. SRUC
255 policy implemented from spring 2015 requires gathered lambs with clinical plochteach to be
256 housed, with their mothers, until they have recovered. Lamb losses of unknown cause on
257 West Highland hill farms are considerable and it is likely that some of these losses are due to
258 plochteach.
259
260 There are few data available on plochteach incidence in the UK. Of 69 respondents to
261 a survey in Northern England in 2013, 32 (46%) reported having animals affected with
262 plochteach and nine (13%) with >10 lambs involved[7]. In Norway, studies have identified a
263 10% incidence (Wisløff et al., 2002) and losses in certain flocks grazing *N. ossifragum*
264 pastures where the disease complex occurs. Mysterud et al. (2000), cited by Steinheim et al.
265 (2012), found that 38% of deaths in extensive flocks with high background mortality from
266 disease, environment and predators were directly attributable to plochteach.
267
268 In the absence of good data on the incidence, severity and impact of plochteach, it is
269 only possible to speculate on the potential losses associated with the disease in Scotland. In
270 2006, the National Farmers' Union of Scotland reported farmers losing up to 100 lambs, with
271 several reporting between 20-40 lamb losses a season[8]. At an open day at SRUC Kirkton and
272 Auchtertyre Farms in 2012, the majority of hill farmers polled said that the disease was
273 endemic on their farm with estimates of 10% of lambs typically affected. The farmers

[7] See: Farm Northwest, 2013. Results in from the saut survey.
http://farmnw.co.uk/news/results_in_from_the_saut_survey (accessed 3 July 2015).

[8] See: Photosensitisation survey to track sheep illness. Stackyard News.
http://www.stackyard.com/news/2006/09/veterinary/03_nfus_photosensitisation.html (accessed 3 July 2015).

274 believed strongly that incidence varied with year and that there was a low incidence in
275 Scotland in 2012, although in England's Lake District (M. Sanderson, personal
276 communication) and Norway (M.J. Ulvund, personal communication) 2012 was considered a
277 year with high incidence.
278
279 As with other cases of poisoning (Guitart et al., 2010) under extensive management
280 systems, disease surveillance laboratories and veterinary surgeons see plochteach only rarely,
281 which means very little quantitative data is collected. Most farmers who see plochteach
282 routinely within their flocks appear to be resigned to it.
283
284 **Prevention**
285 There is currently little or no guidance on how to prevent plochteach in sheep in
286 Scotland other than by avoiding pastures containing *N. ossifragum*. Reducing the incidence by
287 fencing off areas with *N. ossifragum* is impractical as the plant is often ubiquitous.
288 Completely removing sheep from areas where the plant grows from late spring to mid-
289 summer may be possible on some farms with areas of improved pasture[9]. Bringing animals
290 indoors during the day and only allowing night-time grazing may be an option for some
291 (Henderson, 1990) but would presumably only prevent clinical signs, not liver damage.
292
293 *Land management options to reduce the abundance of bog asphodel (Narthecium ossifragum)*
294 Drainage, phosphorus applications (Laksesvela and Dishington, 1983), herbicide
295 application and shading (e.g. by planting trees) reduce the cover of *N. ossifragum* but are
296 technically difficult, hugely expensive and impractical. In the UK such land management

[9] See: Farm Northwest, 2012. Fell farmers share poisonous plant experience. http://farmnw.co.uk/news/saut_disease_are_you_affected_and_looking_for_answers (accessed 3 July 2015).

would require Environmental Impact Assessments[10], and are unlikely to be permitted on large areas of semi-natural vegetation. Given that there is equivocation about the cause(s) of plochteach, such management techniques to remove *N. ossifragum* are unrealistic. See Fig. 2.

*Animal breed differences, genetic and management interactions*

There are many and widespread differences between livestock breeds and genotypes to disease susceptibility and mortality (Steinheim et al., 2012). Many livestock diseases, including a range of mycotoxin-based diseases, show heritable variation for susceptibility to toxins (Bishop and Morris, 2007). Sheep breeds vary in their susceptibility to photosensitisation (Henderson, 1990; Flåøyen, 1991, 1993) and it is likely that variation also exists between individuals of the same breed. Laksesvela and Dishington (1983) found that Norwegian lambs with haemoglobin type AA were significantly more resistant to plochteach than those with type BB, which could be an avenue worth pursuing.

If evidence for within breed genetic variation for susceptibility to plochteach is found, genetic solutions could be sought. However, as a definitive aetiopathogenesis is unknown, and because the incidence varies considerably from year to year, characterising resistant and susceptible populations will be challenging. Animals that are free from disease may simply not have been exposed to the causal agent(s).

We suggest that the most practical method would be to initially select for two lines, namely, susceptible animals and resistant/unexposed animals. Semen samples for artificial insemination (AI) could be collected from ram lambs that have had clinical signs of plochteach, as well as from those with no clinical signs, before they are slaughtered. If liver

[10] See: Scottish Statutory Instruments, 2006. The environmental impact assessment (Scotland) amendment regulations. http://www.legislation.gov.uk/ssi/2006/614/contents/made (accessed 3 July 2015).

pathology does not heal completely between outbreak (June/July) and slaughter (October/November), liver autopsies could be used to identify individuals that have had sub-clinical disease. Genetic gain would be limited by the variation in incidence, since in some years a very small number of animals appear to be affected. If susceptibility to plochteach proves to be sufficiently heritable, traits or genes could be sought that differed from those of the sheep in the resistant/unexposed line. This could provide a start point for genomic studies in parallel with investigations into the pathophysiology of the disease.

**Facial eczema**

Facial eczema (FE), or pithomycotoxicosis, a secondary photosensitisation disease found in New Zealand (Towers, 2006; Morris et al., 2013), may provide a template for addressing plochteach. FE is caused by a toxin, sporidesmin A, in spores of the fungus *P. chartarum*. The toxin causes liver damage and blocks bile ducts resulting in photosensitisation of lambs, adult sheep (Ford, 1974) and cattle (Morris et al., 2009, 2013), but sometimes presents in ewes solely as reduced fertility (Jagusch et al., 1986). Incidence of FE has been successfully reduced in New Zealand by selective breeding (Morris et al., 2004, 2013). In a field challenge in the early 1990s, after about 15 years of selection, 53% of the control line but only 7% of the resistant line were susceptible to FE (Morris et al., 1994), and genetic gain has continued at 2% per year (Amyes and Hawkes, 2014).

By identifying FE resistant rams using quantitative genetic techniques, disease incidence has been successfully reduced in a long-term selection flock. FE resistant sheep have lower growth rates than susceptible sheep, but the programme has demonstrated the net benefits of selection. When unchallenged by sporidesmin, FE resistant lambs were 6% lighter than susceptible lambs at weaning (Morris et al., 1999) but in a moderate FE outbreak, the

346 loss in lamb weight from susceptible sheep was estimated at 13 % (Smeaton et al., 1985). As
347 there are also negative effects on ewe fertility in challenged susceptible sheep (Morris et al.,
348 1991), there is a net benefit to using FE resistant rams in areas where there is regularly a high
349 fungal spore count of *P. chartarum*.

350 A tolerance testing service challenges rams with the toxin and then tests serum
351 gamma-glutamyl transferase (GGT); heritability of the response to sporidesmin was found to
352 be 0.45 (Morris et al., 2013). Serum GGT (collected 2-3 weeks after administration of the
353 toxin) was positively correlated with liver damage scores (Towers and Stratton, 1978) and the
354 relationship was confirmed even for lambs with different levels of genetic susceptibility to FE
355 (Morris et al., 2002). The response to a challenge with sporidesmin is therefore a good
356 indication of predisposition to FE.

357

358 Although significant quantitative trait loci on the genome have been discovered, the
359 overall percentage of variance is low (Phua et al., 2008) and work is now in progress towards
360 using genomic selection for FE resistance. The best genomic prediction equation so far has an
361 average accuracy of 0.38 (Phua et al., 2014), about one-half of the accuracy achieved using
362 the current estimated breeding value (EBV) based on performance testing for FE. Ram
363 breeders can therefore perform a two-stage selection: first using a genetic screen to indicate
364 sporidesmin-tolerant rams, then artificially challenging to double-check for disease resistance
365 and to identify elite animals. Farmers who are getting rams genotyped for other traits can also
366 now identify those animals most susceptible to FE.

367

368 This is a possible approach towards reducing the incidence of plochteach. However
369 the heritability and variation within a population for susceptibility to plochteach need to be
370 established and the toxin(s) isolated in order to conduct challenges as with sporidesmin in FE.

## Factors that have inhibited progress

Much research has focused on laboratory analysis of the plant or attempts to induce the disease in animals under controlled conditions and of the few well conducted field trials conflicting results have been obtained. The discovery of the aetiopathogenesis of FE in New Zealand was impeded by the 7-20 day time lag between exposure to the toxin and development of clinical signs (di Menna et al., 2009); there is probably also a lag between exposure and visible disease in plochteach.

Aetiological uncertainties are exacerbated by the nature of hill farming; sheep come into contact with the toxins in remote areas where there is infrequent human contact. Deaths are frequently unseen because of the extensive nature of the system and because carcasses are rapidly eaten by scavengers (Hewson, 1984). Any form of field study would be challenging not least since the number of animals affected with liver damage but with no clinical signs is unknown.

## Recommended research action

From our review of the literature we recommend that fundamental and applied research is required. Determining the disease aetiology is an important research goal as success would allow a breeding programme to challenge rams with the toxin, so speeding up the process of selecting resistant animals. A natural study of the disease incidence and severity on a large number of farms with extensive pastures containing *N. ossifragum* could be conducted but it would be difficult to determine the number of viable lambs born and such an investigation would be affected by confounded animal genetics and management across farms. The approximate scale of the economic and animal welfare losses (and also possible

meat quality losses) across an appropriate sample of farms needs to be assessed alongside estimates of possible gains from partial mitigation of the disease.

There is a requirement to assess whether patterns of liver pathology, clinical signs and responses to treatment are consistent across farms. It remains unclear whether lambs that have survived plochteach show liver pathology post slaughter and whether liver function tests identify animals with sub- or pre-clinical plochteach; if not, development of a new blood test is required. Field-use biomarkers (either biochemical or genetic) need to be identified that can be used to predict photosensitisation risk and support studies that monitor visual clinical signs.

Better knowledge of the biochemistry of the disease may lead to new curative or preventative options even if the full aetiology remains unclear. Phenotypic data collection has started at SRUC Kirkton and Auchtertyre Farms using its Scottish Blackface long term index flock. Once sufficient data have been amassed we will be better able to assess whether there is within-breed genetic variation in susceptibility to plochteach. If evidence for this is found, selection work could proceed using quantitative genetics and standard breeding and genomic techniques. Both approaches require linked phenotypic data (performance, disease incidence) and pedigree information (sire, dam, and offspring). The quantitative genetics approach would involve selecting for disease susceptibility/resistance or for correlated traits, which could be physical or biochemical. The genomic approach would seek correlations between genomic information and performance or resistance traits and then select susceptible/resistant sheep by breeding animals using genomic information such as markers. To identify traits or markers and demonstrate their impact, both the quantitative genetics and genomic approaches would require flocks with full parentage data where plochteach regularly occurs in a significant

proportion of lambs. The availability of pedigree information would allow genetic correlations to be estimated between current production traits, potential markers and plochteach resistance.

There would also be the option to develop EBVs for plochteach resistance, similar to those currently available for worm resistance, or in development for footrot in the UK (Conington et al., 2008). Design of such work would need to consider potential heritabilities, levels of incidence of clinical signs, and different levels of challenge. Until the causal agent(s) are identified, levels of challenge could be manipulated by controlling the amount of time animals spend on boggy ground. A multi-year, multiple sire dataset is needed and would be the first conditional stage towards seeking a genetic solution.

## Conclusions

Pragmatic research is required to reduce the incidence and severity of plochteach before working towards identifying the cause(s). The disease affects young lambs, causing physical damage, reduced production and/or death; it occurs in the presence of *N. ossifragum* but control of the plant is neither practical nor cost effective. There appear to be genetic and/or phenotypic factors in sheep that affect the incidence and severity of the disease but there are no reliable statistics on the distribution, scale and cost of the disease in UK. While localised to parts of North-West Europe, plochteach can have a major impact on individual animals and flocks. Ongoing upland peatland ecosystem remedial works are likely to result in an increase in the abundance of *N. ossifragum* and consequently a possible increase in the disease incidence. Working towards breeding plochteach resistant animals and understanding more about the disease complex are therefore desirable from both future animal welfare and upland farming system economic perspectives.

## Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.


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879 **Table 1** Examples of photosensitisation diseases in animals. Primary photosensitisation is caused directly by the ingestion of photodynamic compounds; secondary
880 photosensitisation by liver damage resulting in failure to excrete phylloerythrin, a photodynamic compound.
881

| Type | Name | Cause of photosensitisation | Comments | References |
|---|---|---|---|---|
| Primary | | Plant: Perforate St. John's-wort (*Hypericum perforatum*)<br>Toxin: hypericin | | Marsh and Clawson (1930); Araya and Ford (1981); Bourke (2000); Cheeke (1995) |
| | | Plant: Buckwheat (*Fagopyrum esculentum*)<br>Toxin: fagopyrin | Cultivated in Europe, Asia and USA | Cheeke (1995) |
| | | Plant: forage rape (*Brassica napus*) | | Collett et al. (2014) |
| | Plochteach | Cyanobacteria? | | Tønnesen et al. (2010), Tønnesen et al. (2013) |
| Secondary | Plochteach (Alveld, yellowses, head-greet, saut) | Suspected plant: Bog asphodel (*Narthecium ossifragum*)<br>Suspected toxins: steroidal sapogenins and saponins<br>Other hypothesised agents: cyanobacteria | | Flåøyen (1993)<br><br>Tønnesen et al. (2010), Tønnesen et al. (2013) |
| | Facial eczema | Fungus: *Pithomyces chartarum*<br>Toxin: Sporidesmin | Fungus present at the base of pasture.<br>Affects small ruminants and dairy cattle in New Zealand.<br>Also reported in Turkey. | Morris et al. (2004)<br><br>Ozmen et al. (2008) |
| | | Plant: Ragwort (*Senecio* spp.).<br>Toxin: pyrrolizidine alkaloids | S. America | Giaretta et al. (2014) |
| | Geeldikkop | Plant: Puncture vine (*Tribulus terrestris*)<br>Toxin: steroidal sapogenin | Affects small ruminants of Australia and South Africa (also California, Argentina). | McDonough et al. (1994); Kellerman et al. (1991; 1996) |
| | | Plant: Kleingrass (*Panicum coloratum*) | Texas | Bridges et al. (1987) |
| | | Plant: Sacahuiste (*Nolina texana*) | Texas | Mathews (1940) |
| | | Plant: Littleleaf horsebrush (*Tetradymia glabrata*) | Canada, western USA | Johnson (1974) |
| | | Plant: Signal grass (*Brachiaria decumbens*) | Brazil, Africa | Gomar et al. (2005) |
| | | Plant: *Lantana camara* | India | Kumar et al. (2009) |
| | | Parasite: Lancet liver fluke (*Dicrocoelium dendriticum*) | Scotland (Island of Coll) | Sargison et al. (2012) |
| | | Cyanobacteria: *Nodularia* spp., *Microcystis* spp. | South Africa | van Halderen et al. (1995) |
| | | White liver disease (resulting from severe Cobalt deficiency) | Australia, Switzerland, UK | Richards and Harrison (1981); Tontis and Meier (1998); Dannatt and Porter (1996) |
| Genetic defect | | Heritable genetic defects in Southdown and Corriedale sheep | | Corneliu and Gronwall (1968); Corneliu et al. (1965) |

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**Figure legends**

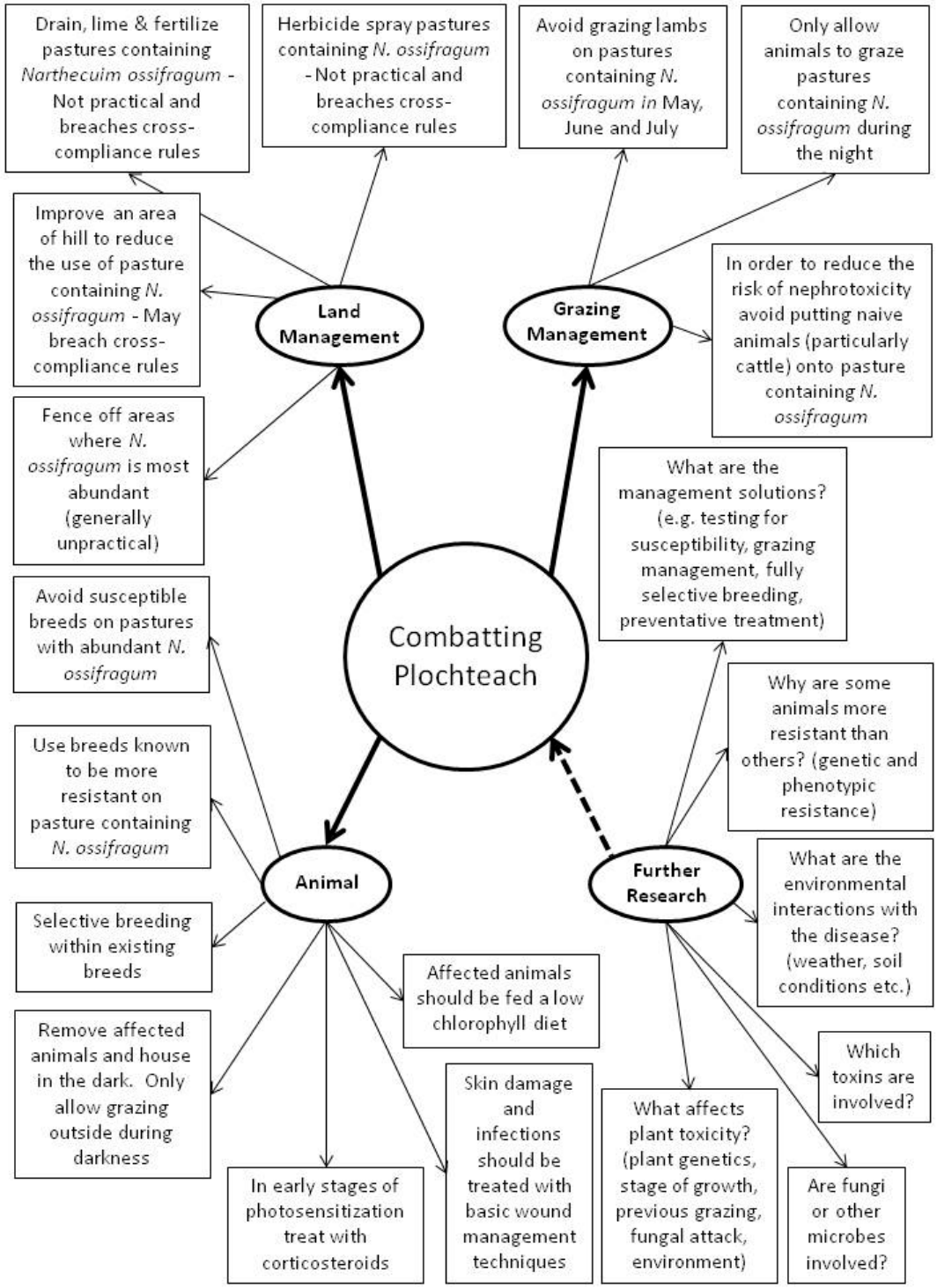
Fig. 1. Bog asphodel (*Narthecium ossifragum*) (A) leaves and (B) flowers. Leaves are 2-5 mm wide; flower stems are 5-45 cm tall.

A

B

897 Fig. 2. Potential methods of controlling the disease and further research that is needed to fully

898 understand the disease.

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